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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
STUCKER, JEFFREY J	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 05/22/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/642,763	VEAS, FRANCISCO	
	Examiner	Art Unit	
	Jeffrey Stucker	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 22-45 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 22-45 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/19/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

The specification is objected to for the following informalities:

The specification is objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID Nos. to all mentions of specific sequences in the specification and the claims. See 37 CFR § 1.821(d).

Appropriate correction is required.

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim 41 is objected to for poor grammar of "A serums": "A" is for singular forms of the noun.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 22-24, 33, 35, 37-39, 44, and 45 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 is vague and indefinite. The phrase "and particularly" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 24 is not clear in what is meant by "vectors expressing the target receptor(s) on their surface". Vectors are DNA segments that normally do not express receptors.

Claim 33 is confusing and unclear because yeast are not viral vectors. In addition, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claims 35 and 37 are vague. Are the gp120 and gp160 from HIV-1? What are "preserved regions"?

Claim 38 is vague and indefinite: Replaced by a monoclonal antibody specific for what? Will any monoclonal antibody do?

Claim 39 is vague and indefinite. What is "recombining form"? What are "preserved regions" of proteins? What is "recombining form"? In addition, the phrase "possibly" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 39 is rejected because claim 22 requires means "expressing" receptor and pathogen, whereas claim 39 is only the specific proteins, not a means expressing the proteins.

Claims 44 and 45 do not make any sense because the group from which the virus is chosen is not a list of viruses.

35 U.S.C. § 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claim 41 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claim 41 is a product of nature by virtue of not being an isolated and purified serum or antibody. The claim reads on the antibodies as they exist in an inoculated animal.

Claims 22 and 42 are rejected under 35 U.S.C. § 101 because the invention as disclosed is inoperative and therefore lacks patentable utility.

The invention is directed to a vaccine composition in general and a vaccine against HIV. Thus, the ultimate utility of the instant invention would be whatever the ultimate utility of the identified molecules is. Based upon the disclosure, as well

as the nature of HIV, it is clear that the specification envisions a pharmaceutical utility for these compounds in humans.

While the specification does contain statements regarding the use of the invention as a vaccine, the specification fails to teach, nor does it describe such use. The difficulties inherent to development of an HIV vaccine are well known and some of which are noted in the disclosure. Specifically, "The extraordinary ability of HIV to mutate, the inability of many currently known specificities of anti-HIV antibodies to consistently neutralize HIV primary isolates, and the lack of a complete understanding of the correlates of protective immunity to HIV infection have impeded efforts to develop an HIV vaccine having the desired effectiveness."

Other concerns that need to be addressed are:

1) the extensive genomic diversity associated with the HIV retrovirus, due in large part to error prone reverse transcription of its single-stranded RNA genome,

2) the fact that the modes of viral transmission include virus-infected mononuclear cells, which pass the infecting virus to other cells in a covert form (cell to cell transmission), as well as via free virus transmission,

3) the existence of latent forms of the virus (i.e., beyond the blood-brain barrier),

5) the complexity and variation of the elaboration of the disease and,

6) the property of some portions of HIV proteins or peptides to actually cause immunosuppression or other detrimental consequences.

The existence of these obstacles prevents one of ordinary skill in the art from accepting any vaccine or immunization treatment or any therapeutic regimen on its face. In order to provide proof of utility with regard to drugs and their uses, either clinical or *in vivo* or *in vitro* data, or a combination of these can be used. However, the data must be such as to convince one of ordinary skill in the art that the proposed utility is sufficiently established. See *in re Irons*, 340 F.2d 924, 144 USPQ 351 (CCPA 1965), *Ex parte Krepelka*, 231 USPQ 746 (PTO Bd. Pat. App & Inter. 1986) and *Ex parte Chwang*, 231 USPQ 751 (PTO Bd. Pat. App & Inter. 1986). Applicant's disclosure does not provide evidence of having invented an HIV vaccine.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 24 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

"[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation.'" *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *Amgen Inc. v. Chugai Pharm. Co.*, 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re Fisher* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman* [230 USPQ 546, 547 (BdPatAppInt 1986)]. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)

the predictability or unpredictability of the art, and (8) the breadth of the claims.

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).

It is not clear what is meant by "vectors expressing the target receptor(s) on their surface". Vectors are DNA segments that normally do not express receptors. if this in deed is what Applicant intends, there are no teaching in the specification as to how one would accomplish this.

Claims 22 and 42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an immunogenic composition, does not reasonably provide enablement for a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant invention is drawn to a vaccine composition but the specification does not sufficiently support the full scope

of the claimed vaccine. The term "vaccine", by definition, implies a preparation intended for active immunological prophylaxis; e.g., preparations of killed microbes of virulent strains or living microbes of attenuated (variant or mutant) strains; or microbial, fungal, plant, protozoa, or metazoan derivatives or products. Although nearly any protein when inoculated can cause an immune reaction, the prophylactic nature of this reaction is not guaranteed and has to be experimentally determined. Prophylaxis is defined as the prevention of disease or of a process that can lead to disease. For example, the *Illustrated Dictionary of Immunology* defines vaccine as a composition that stimulates protective antibodies and T cell immunity and induces active immunity. Paul in *Fundamental Immunology* teaches that vaccines were developed primarily as a prophylactic measure to prevent disease. This is achieved by use of an antigenic (immunogenic) agent to actively stimulate the immunological mechanism, or the administration of chemicals or drugs to members of a community to reduce the number of carriers of a disease and to prevent others from contracting the disease. Testing protocols are designed to test the efficacy of the vaccines which include challenge trials or natural exposure to the disease agent in an endemic area. Further, he teaches that there is not always a correlation between seroconversion and

protection from disease. Given the teachings in the art, it is clear that a compound that merely induces an immune response is not sufficient but must be protective to qualify as a vaccine. See at the top of page 1312: "[T]here was not always a correlation between seroconversion and protection from disease...." There are no challenge studies with wild type virus.

The ability of a vaccine to raise a protective immune response depends on the structure of the protein epitopes. Paul teaches that to determine the immunogenicity of certain regions of a protein, knowledge of the three dimensional structure of the protein is required to determine which polypeptides in a given protein would be accessible on the surface of the protein in order for the putative antigenic determinant to be bound by the antibody. In addition, Paul states that mobility of the putative antigenic determinant within the native protein structure is also a determining factor for the binding of the antigenic determinant to an antibody. Paul points out (page 250, lines 4-8) that "Measurement of the mobility in the native protein is largely dependent on the availability of a high resolution crystal structure, so its applicability is limited to only a small subset of proteins." Riffkin et al. (*Gene*, 1995) teaches that a single amino acid change can alter the structure

of the protein dramatically. Abaza et al. (*J. of Protein Chemistry*, 1992) teaches that mutations outside of the antigenic epitope exert an effect on the structure of the epitope. Because the structure of the protein determines its antigenicity and thereby its function as a vaccine, these structures cannot be predicted. In regards to the factors cited in the lack of utility rejection, Cohen et al. recognize other problems: "No vaccine capable of eliciting protective immunity to HIV infection has been formulated. HIV presents a formidable challenge to immune surveillance based on many factors, including hypervariability of its principal neutralizing domain (V3), concealment of critical, functional domains in the external envelope glycoprotein (gp120) behind inessential structures, and infection of APCs resulting in their dysfunction. Substantial progress has been made recently in defining neutralizing domains within the HIV envelope, and in augmenting the immune response to HIV proteins. Despite these important advances, an effective HIV vaccine remains elusive, we propose, because the immediate immunodeficiency accompanying HIV infection creates another obstacle to a successful vaccine." Applicant's specification does not address these factors and does not disclose that the instant invention has overcome these problems.

Given the uncertainty in the vaccine art as demonstrated by the references and the lack of working examples in the instant specification, the instant application is not enabled for vaccines.

The instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 22, 24, 26-37 and 41 are rejected under 35 U.S.C. § 102(b) as being anticipated by LaCasse et al.

The instant invention is an immunogenic composition comprising "means" expressing a receptor and a second "means" expressing at least the receptor binding portion of the pathogenic agent. The means can be cells or vectors.

Claims are product-by-process claims and are not limited to the manipulations of the recited steps, only the structure implied by the steps. See MPEP § 2113:

> "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

LaCasse et al. teach cells that express receptors for HIV and cells that express HIV gp120 that are fused to freeze exposed cryptic epitopes for immunization purposes. Therefore, given that the claims are directed to a composition, the instant invention is anticipated by LaCasse et al.

Claims 22, 26, 29, 30, 36, and 37 are rejected under 35 U.S.C. § 102(a) as being anticipated by Schønning et al.

The search report describes the reference as an "X" reference which is an anticipatory teaching, and therefore, falls within 35 U.S.C. § 102. The instant application is not accorded the priority date of French patent 99 01 794 because no English translation is available in the instant application.

Claims 22, 31, 38, 39, and 41 are rejected under 35 U.S.C. § 102(a) as being anticipated by DeVico et al.

The claims are directed to a first means comprising soluble gp120 and a second means comprising soluble CD4 and a monoclonal antibody.

DeVico et al. teach soluble gp120 bound to soluble CD4 forming a complex which in turn is bound by a monoclonal antibody, thereby meeting the claims. Therefore, the instant invention is anticipated by DeVico et al.

Claims 22, 31, 38, 39, and 41 are rejected under 35 U.S.C. § 102(a) as being anticipated by Kwong et al.

The claims are directed to a first means comprising soluble gp120 and a second means comprising soluble CD4 and a monoclonal antibody.

Kwong et al. teach soluble gp120 bound to soluble CD4 forming a complex which in turn is bound by a monoclonal antibody, thereby meeting the claims. Therefore, the instant invention is anticipated by Kwong et al.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 22, 25, and 41 are rejected under 35 U.S.C. § 103(a) as obvious over DeVico et al. or Kwong et al., both in view of Rigaud et al.

The instant claims are directed to using liposomes to display viral proteins and cell surface receptors.

The relevance of DeVico et al. and Kwong et al. is given above. Rigaud et al. teach that it is routine and well known in the art how to place proteins on the surface of liposomes. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the liposomes of Rigaud et al. to anchor the soluble proteins of the primary references to better mimic the structure of the proteins and their interactions by placing them into a cell-like structure. Therefore, the instant invention is obvious over DeVico et al. or Kwong et al., both in view of Rigaud et al.

Claims 22 and 40 are rejected under 35 U.S.C. § 103(a) as obvious over LaCasse et al. in view of Rossio et al.

The claimed invention is directed to cross-linking the first and second means with AT-2.

The relevance of LaCasse et al. is set forth above. Rossio et al. teach the non-denaturing binding of HIV surface proteins using AT-2. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute AT-2 for formaldehyde for the advantage of this non-denaturing binding relative to denaturing binding agents such as formaldehyde as taught by Rossio et al. Therefore, the instant invention is obvious over LaCasse et al. in view of Rossio et al.

Claims 22-24, 26-40, and 41 are rejected under 35 U.S.C. § 103(a) as obvious over LaCasse et al. in view of Riley et al.

The relevance of LaCasse et al. has been set forth above. Riley et al. teaches infecting human cells with HIV. It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute human cells and HIV as the starting means for creating the antigen. The infection would exactly match the natural course of infection and would be expected to result in epitopes that mimic actual epitopes during

natural infection. Further, if one were to raise antibodies in a mammal, one would expect that autologous cells as antigens would minimize the risk of microbial infection from a different donor as well as limiting the immune reaction to the new epitopes, rather than all of the antigens on the cells as would happen from a different donor. Therefore, the instant invention is obvious over LaCasse et al. in view of Riley et al.

No claims are allowed.

Papers related this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989).

The Group 1600 Official Fax number is: (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Stucker whose telephone number is (571)-272-0911. The examiner can normally be reached Monday to Thursday from 7:00am-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell, can be reached on (571)-272-0974.

JEFFREY STUCKER
PRIMARY EXAMINER